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PROSPECTIVE ANALYSIS

Effect of regular physical activity and lifestyle changes on insulin resistance in patients after kidney transplantation

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ABSTRACT
Insulin resistance (IR) is the most significant risk factor for post-transplant diabetes mellitus (PTDM). This study aimed to determine the effects of regular physical activity on IR and PTDM in patients after kidney transplantation (KT). The study group (n = 22) participated in aerobic or combined sports (aerobic and anaerobic). Monitoring was provided by a sports tracker (Xiaomi Mi Band 4, compatible with the Mi Fit mobile application). Waist circumference was significantly lower (p = 0.0437, p = 0.0372), graft function was better (p = 0.0036, p = 0.0137), fasting blood glucose was lower (p = 0.0016, p = 0.0003), C-peptide level was lower (p = 0.0447, p = 0014) in the 3rd and 6th months of monitoring, and low-density lipoprotein was lower at 6 months (p = 0.0444) in the observed group than in the control group. IR was significantly lower at 6 months (p = 0.0202), and fasting blood glucose was significantly lower at 3 and 6 months (p = 0.0227) in the observed group. We confirmed the significant effect of regular physical activity on preventing the development of IR and impaired fasting glucose levels in patients after KT *(Tab. 1, Fig. 4, Ref. 27)*. Text in PDF *www.elis.sk*
KEY WORDS: kidney transplantation, insulin resistance, physical activity.

Introduction

Patients After kidney transplantation (KT), have a higher incidence of insulin resistance (IR) compared to the age- and sex-matched general population (1). IR is the most important predictor of post-transplant diabetes mellitus (PTDM), which was confirmed in a multicenter study of KT recipients in the Slovak Republic (2). Similar to type 2 diabetes mellitus (DM), the pathogenesis of PTDM is associated with impaired insulin-mediated glucose uptake by peripheral tissues, as well as impaired insulin-mediated suppression of liver glucose release. In their study using a hyperinsulinemic-euglycemic clamp, Danish et al found a decrease in insulin sensitivity six months after KT, which was characterized by impaired suppression of endogenous glucose production and excretion in the liver and whole-body lipolysis (3). However, IR itself is not manifested by hyperglycemia as long as B cells are able to compensate; therefore, their dysfunction is probably necessary to bridge PTDM (4).

Insulin resistance plays an important role in the development of cardiovascular diseases (5). Cardiovascular morbidity and mortality significantly limit long-term survival of patients after KT. The incidence and prevalence of cardiovascular diseases were five times higher in this group than in the general population (6). It appears that patients with impaired glucose tolerance in the post-transplant period have the same risk of mortality as patients with confirmed PTDM (7). The main risk factors of IR after KT are weight gain, obesity, low physical activity, and chronic immunosuppressive therapy. Oterdoom et al. confirmed that obesity, its distribution, and prednisolone dose are fundamental determinants of long-term IR after KT (6). Intense lifestyle changes, decreased caloric intake, weight reduction, and exercise are well-established steps to prevent pre-diabetic conditions and type 2 DM with long-lasting effects in non-transplant populations (8, 9). The active influence of modifiable risk factors may be key in preventing the development of IR after KT.

Physical activity is one of the most important steps people of all ages can take to improve their health. A sedentary lifestyle can affect patients at all stages of chronic kidney disease (CKD), including KT (10). Low physical activity has been identified as a major modifiable risk factor of mortality in patients with end-stage CKD (11). KT offers these patients the elimination of factors

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Abbreviations: ADA – American Diabetes Association, ADPKD – autosomal dominant polycystic kidney disease, BMI – body mass index, CKD – chronic kidney disease, CKD-EPI – Chronic kidney disease-Epidemiology Collaboration Index, CMV – cytomegalovirus, DGF – delayed graft function, DM – diabetes mellitus, eGFR – estimated glomerular filtration rate, FPG – fasting plasma glucose, FPI – fasting plasma insulin, GNF – glomerulonephritis, $HbA1_c$ – glycated hemoglobin, HDL – high-density lipoprotein, HOMA-IR – Homeostatic Model Assesment of Insulin Resistance, HRmax – maximum heart rate, IR – insulin resistance, IRI – immunoreactive insulin, KDIGO – Kidney disease: Improving Global Outcome, KT – kidney transplant, LDL – low-density lipoprotein, M – month, oGTT – oral glucose tolerance test, PTDM – post-transplant diabetes mellitus, TAG – triglycerides, TIN – tubulointerstitial nephritis, WHO – World Health Organization

that contribute to a sedentary lifestyle, such as time spent on dialysis, anemia, uremia, and reduced production of certain hormones (12). The effects of insulin on the liver and muscles can be modified through regular physical exertion. Regular training increases muscle capillary density, oxidative capacity, and lipid metabolism, and supports insulin signaling pathways. If the primary objective is to improve the effects of insulin, then moderate- or high-intensity activities are optimal. The most significant improvement was observed in patients with the highest baseline IR (13).

The 2009 KDIGO (Kidney Disease: Improving Global Outcome) recommendations for the treatment of patients after KT contain only vague guidelines in which these patients are strongly encouraged to follow a healthy lifestyle through exercise, proper diet, and weight reduction as needed (14). Few studies have addressed this issue based on subjective self-assessment questionnaires, and they are usually uncontrolled. This study aimed to determine the effect of regular physical activity on the prevention of IR and other risk factors (hyperlipidemia, fasting hyperglycemia, and weight gain) of PTDM in patients after KT. The secondary goal was to evaluate its effect on graft function. Specificity of sports activities was objectively monitored using digital technology.

Materials and methods

This was a prospective, controlled analysis. The study group consisted of patients (n = 44) who underwent primary living donor or deceased donor KT at the Martin Transplant Center. The total duration of follow-up was 6 months, and all patients underwent three examinations during the follow-up period: at admission, at 3 months, and at 6 months.

Patients with good stable graft function at least 3 months after KT, defined by an estimated glomerular filtration rate (eGFR) of ≥ 60 ml/min/1.73 m^2 according to the Chronic Kidney Disease Epidemiology Collaboration Index (CKD-EPI), were included in the cohort. Exclusion criteria were diagnosis of DM, PTDM, prediabetic conditions (fasting hyperglycemia, impaired glucose tolerance), age over 65 years, and hemoglobin level < 100 g/l. All the patients received the same combination of immunosuppressive drugs in the maintenance regimen (tacrolimus, mycophenolic acid, and prednisone). The files were then divided into two groups.

All patients completed an initial interview before enrollment in the study. Interviews focused on lifestyle, diet, and physical activity. Patients who engaged in regular physical activity were excluded from the study.

The intervention group consisted of 22 patients for whom a limit of at least 150 min of moderate exercise per week was established. This limit is based on the 2016 recommendations of the American Diabetes Associaton (ADA) for the prevention and treatment of DM and prediabetic conditions in the general population (15). At the same time, patients were advised not to take a break of more than two days between exercises. The type of activity allowed was aerobic (running, swimming, brisk walking, cycling) or combined (aerobic + strength) physical activity, according to the patient‘s preferences. Physical activity was monitored using a Xiaomi Mi Band4 sports bracelet compatible with the Mi Fit mobile application, where the characteristics of the activity performed were stored for the entire monitored period (duration and frequency per week, total energy expenditure, type of sports activity, and heart rate). The intensity of physical activity was assessed using the% of maximum heart rate (HRmax), which was determined using a simple scheme: 220 patients. The level of physical activity of medium intensity represents 64–76% of HRmax and of high intensity 77–93% (16). A control group (n = 22) was created for the intervention group, whose members met all the inclusion and exclusion criteria of the study and matched the control group in terms of average age, type of immunosuppression, and kidney function. These patients were instructed on routine measures while maintaining stable body weight and waist circumference through an active lifestyle and diet. However, compared with Group 1, they were not prescribed a minimum level of physical activity and were not monitored during follow-up. The participants completed a questionnaire describing their lifestyle at the end of the study. None of the patients in the control group met the criteria for the intervention group’s exercise limit per week during the study period.

The parameters recorded for each patient are presented in Supplementary Table 1. Laboratory and anthropometric parameters were monitored during each outpatient check-up. To evaluate IR, we used the insulin resistance index from the homeostatic model (HOMA-IR), which is calculated by multiplying the values of fasting plasma glucose (FPG) and fasting insulin (FPI) divided by 22.5, and thus HOMA-IR = (FPG x FPI)/22.5. Proteinuria was examined by 24-hour urine collection. Input parameters included a history of cytomegalovirus (CMV) replication (cut-off point of 1000 cop/ml) that required transient reduction or discontinuation of mycophenolic acid and 21-day treatment with valganciclovir. All patients had stable fasting tacrolimus levels maintained in the recommended range of 3.0–6.0 ng/L during the follow-up period. The daily prednisone dose in both groups was regularly recorded. A positive family history of DM indicated a confirmed occurrence in the siblings, parents, and grandparents.

Finally, the monitored group was divided into four subgroups according to the level of physical activity (duration and intensity): 1) met only the primary endpoint (≥ 150 min, medium intensity) and 2) ≥ 150 minutes and fifty minutes, high intensity; 3) ≥ 300 min, medium intensity; 4) ≥ 300 min and high intensity. We also divided physical activity into two subgroups: a) aerobic activity and b) combined activity. We compared the HOMA-IR and other monitored characteristics between the individual subgroups.

The certified statistical program MedCalc, version 13.1.2. (MedCalc Software VAT registration number: BE 0809 344,640; Member of the International Association of Statistical Computing, Ostend, Belgium). For basic characteristics, the mean, median, and standard deviation were used. Comparisons of continuous variables between groups were performed using parametric (t-test) or non-parametric (Mann–Whitney) tests. Associations between categorical variables were analyzed using the c^2 test

Tab. 1. Group characteristics.

Group characteristics	Monitored group n = 22	Control group n = 22	p
Basic group characteristics			
Gender – men (%)	50	54.5	0.7677
Age (years)	42.6±8.8	42.8±13.2	0.9531
Time after KT (M)	60.6±50 (median 36)	15.8±9 (median 15)	**0.0002**
Basiliximab in induction (%)	36.4	31.8	0.7504
Delayed graft function (%)	4.5	4.5	1.0000
DM positive family history (%)	41	45.5	0.7658
Smokers (%)	9	13.6	0.6338
Anamnesis of CMV (%)	13.6	9.1	0.6418
Anamnesis of acute rejection	18	4.5	0.1613
Average prednisone dose (mg/day)	5.9±2.4	5.5±1	0.4745
Anthropometric data			
Body weight (kg) base line	75±14.3	77±16.4	0.6686
Body weight (kg) 3M	74.9±13.8	78.3±16.4	0.4610
Body weight (kg) 6M	75.1±13.4	79.7±17	0.3246
BMI (kg/m2) base line	25.5±3.2	25.5±3.8	1.0000
BMI (kg/m2) 3M	25.4±3	26±3.7	0.5578
BMI (kg/m2) 6M	25.5±2.9	26.4±4	0.3977
Waist circumference (cm) base line	90.6±12.4	94.1±12.2	0.3507
Waist circumference (cm) 3M	89.3±11.5	96.7±12.1	**0.0437**
Waist circumference (cm) 6M	89.1±11.1	96.7±12.3	**0.0372**
Body height (cm)	171±8.2	173±11.7	0.5150
Laboratory parameters – graft function			
Creatinine (µmol/l) base line	95.1±17.4	101.4±23.3	0.3154
Creatinine (µmol/l) 3M	98.2±19.2	114.5±30.1	**0.0381**
Creatinine (µmol/l) 6M	94.5±22.1	110.1±27.1	**0.0425**
eGFR CKD-EPI (ml/min) base line	76.4±15.5	72.7±18.9	0.4816
eGFR CKD-EPI (ml/min) 3M	74.1±16	63.4±16.3	**0.0036**
eGFR CKD-EPI (ml/min) 6M	78.2±17.5	65.7±14.6	**0.0137**
Quantitative proteinuria (g/l) base line	0.236±0.15	0.220±0.18	0.7503
Quantitative proteinuria (g/l) 3M	0.220±0.19	0.267±0.29	0.5383
Quantitative proteinuria (g/l) 6M	0.187±0.13	0.347±0.42	0.0952
Vitamin D (µg/l) base line	31.9±10.2	23.2±7.2	**0.0022**
Vitamin D (µg/l) 3M	29.5±8.9	24±8	**0.0369**
Vitamin D (µg/l) 6M	27.9±8.8	26.5±10	0.6246
Hemoglobin (g/l) base line	143±12.1	133±15	**0.0193**
Hemoglobin (g/l) 3M	145±10.3	137±16.5	0.0605
Hemoglobin (g/l) 6M	146±11.5	142±16.7	0.3601
Laboratory parameters – glucose metabolism			
Fasting glucose (mmol/l) base line	4.6±0.5	5.2±0.5	**0.0003**
Fasting glucose (mmol/l) 3M	4.8±0.6	5.7±1.1	**0.0016**
Fasting glucose (mmol/l) 6M	4.8±0.6	5.7±0.9	**0.0003**
C-peptide (µg/l) base line	2.5±1	3.1±1.2	0.0788
C-peptide (µg/l) 3M	2.2±0.8	2.8±1.1	**0.0447**
C-peptide (µg/l) 6M	2.4±0.9	4±2	**0.0014**
Immunoreactive insulin – IRI (mU/l) base line	8.4±6.2	7.8±3.2	0.6887
Immunoreactive insulin – IRI (mU/l) 3M	8.3±6.8	7.9±3.4	0.8063
Immunoreactive insulin – IRI (mU/l) 6M	8.7±4.7	9.7±3.7	0.4374
HOMA-IR base line	1.7±1.3	1.8±0.8	0.7601
HOMA-IR 3M	1.8±1.5	2.4±1.2	0.1504
HOMA-IR 6M	1.9±1	2.5±1.1	0.0653
Glycated hemoglobin – HbA1c (%) base line	3.6±0.4	3.8±0.7	0.2512
Glycated hemoglobin – HbA1c (%) 3M	3.6±0.5	3.6±0.5	1.0000
Glycated hemoglobin – HbA1c (%) 6M	3.6±0.5	3.9±0.7	0.1094

Tab. 1. (continued)

Group characteristics	Monitored group n = 22	Control group n = 22	p
Laboratory parameters – lipid profile			
Cholesterol (mmol/l) base line	5±0.8	5.3±1	0.2781
Cholesterol (mmol/l) 3M	4.9±0.8	5.1±1	0.4679
Cholesterol (mmol/l) 6M	4.8±0.8	5.2±1	0.1504
LDL – low-density lipoprotein (mmol/l) base line	2.8±0.7	3.2±0.8	0.0848
LDL – low-density lipoprotein (mmol/l) 3M	2.8±0.7	3±0.9	0.4153
LDL – low-density lipoprotein (mmol/l) 6M	2.7±0.8	3.2±0.8	**0.0444**
HDL – high-density lipoprotein (mmol/l) base line	1.5±0.4	1.3±0.4	0.1047
HDL – high-density lipoprotein (mmol/l) 3M	1.5±0.5	1.4±0.5	0.5107
HDL – high-density lipoprotein (mmol/l) 6M	1.5±0.5	1.4±0.4	0.4679
TAG – triglycerides (mmol/l) base line	2±1.4	2.2±1	0.5885
TAG – triglycerides (mmol/l) 3M	1.5±0.9	1.8±0.7	0.2240
TAG – triglycerides (mmol/l) 6M	1.7±0.8	2±0.9	0.2492

KT – kidney transplant; DM – diabetes mellitus; CMV – cytomegalovirus; BMI – body mass index; M – month; eGFR – estimated glumerular filtration rate; CKD-EPI – Chronic Kidney Disease Epidemiology Collaboration; HOMA-IR – homeostatic model assessment for insulin resistance

and Fisher's exact test, as appropriate. Statistical significance was set at $p < 0.05$.

Results

A total of 44 patients were enrolled in the study, of which 22 were in the monitoring group and 22 were in the control group. Table 1 shows the basic characteristics of each group. There were no significant differences between the two groups in terms of sex ($p = 0.7677$) and age structure ($p = 0.9531$). Patients in the control group had a significantly shorter time from KT than those in the monitored group ($p = 0.0002$), but the mean time interval from KT in this group was 15.8 ± 9 months, thus, the inclusion criterion was met (minimum, 3 months after KT). There were no differences between the two groups in terms of the daily dose of prednisone or basiliximab used in the induction protocol. Chronic glomerulonephritis and tubulointerstitial nephritis were the most common. Of the 22 patients in the monitored group, 15 performed isolated aerobic activity and 7 combined (aerobic + strengthening). The types of sports exercised included running, cycling, brisk walking, hiking, swimming, weight training, and body weight training.

By monitoring anthropometric parameters, we found a statistically significant decrease in waist circumference in the monitored group at 3 ($p = 0.0437$) and 6 months ($p = 0.0372$) after KT compared to the control group. In contrast, we did not observe a significant difference in body weight or BMI between the two groups.

Patients in the control group had a significant increase in creatinine compared to those in the intervention group at 3 ($p = 0.0381$) and 6 months ($p = 0.0425$), and at the same time showed poorer graft function expressed by eGFR according to the CKD-EPI ($P = 0.0036$), $p = (0.0137)$. At the beginning of the follow-up period, the patients had significantly lower levels of vitamin D. This trend continued in the third month of follow-up, but had an increasing tendency; on the contrary, decreasing in the monitored group, and at the end of the follow-up, we did not observe a significant difference in its level. The hemoglobin level was initially lower in the control group, but on average was in the zone of very mild anemia, and therefore met the inclusion criteria. At the same time, it was saturated during the follow-up, and the differences between the groups leveled off.

Differences in glucose and lipid metabolism were also observed. In the intervention group, fasting plasma glucose levels were significantly lower at baseline ($p = 0.0045$), 3 months ($p = 0.0016$), and 6 months ($p = 0.0003$). However, the higher baseline glycemia in the control group fell within the normoglycemic range and did not represent a pathological condition. Furthermore, in the intervention group, we found significantly lower levels of C-peptides at 3 months ($p = 0.0447$) and 6 months ($p = 0.0014$). The lipid profile indicated significantly lower LDL cholesterol levels in this group at the end of the follow-up period ($p = 0.0444$).

We confirmed that there was a significant increase in HOMA-IR in the control group at the end of the follow-up ($p = 0.0202$) (Fig. 1). Fasting blood glucose levels increased significantly in this group as early as 3 months, and a significant difference persisted at the end of the follow-up ($p = 0.0227$) (Fig. 2).

In the monitored group, according to the level of physical activity, seven patients (1st subgroup) met the primary endpoint only, five patients met the conditions of the second subgroup, six patients in the third subgroup, and four patients in the fourth subgroup. No significant differences in HOMA-IR or other glucose and fat metabolism parameters were found between the subgroups. Subgroup 4, with the highest level of physical exertion, showed a significant reduction in waist circumference at the end of follow-up ($p = 0.0173$) (Fig. 3).

We also did not observe a difference in IR between subgroups with isolated aerobic training ($n = 15$) and combined training ($n = 7$). Patients who practiced only aerobic activity achieved a significant decrease in triglyceride levels at the end of follow-up ($p = 0.046$) (Fig. 4).

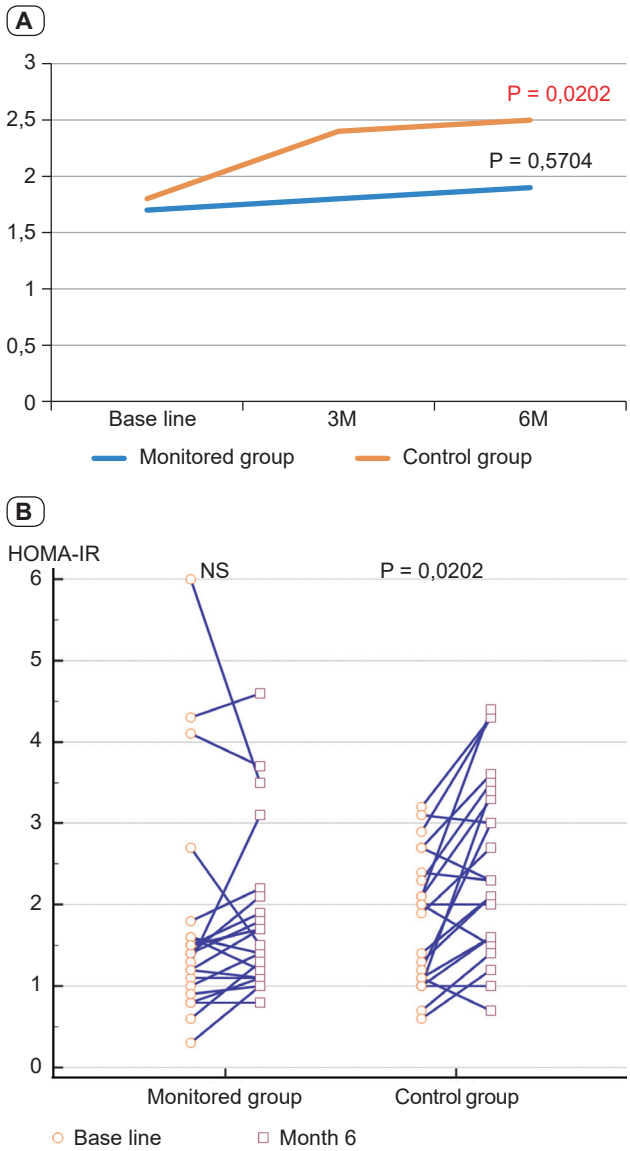

Fig. 1. Development of HOMA-IR during the study – A: whole group B: individually. M – month.

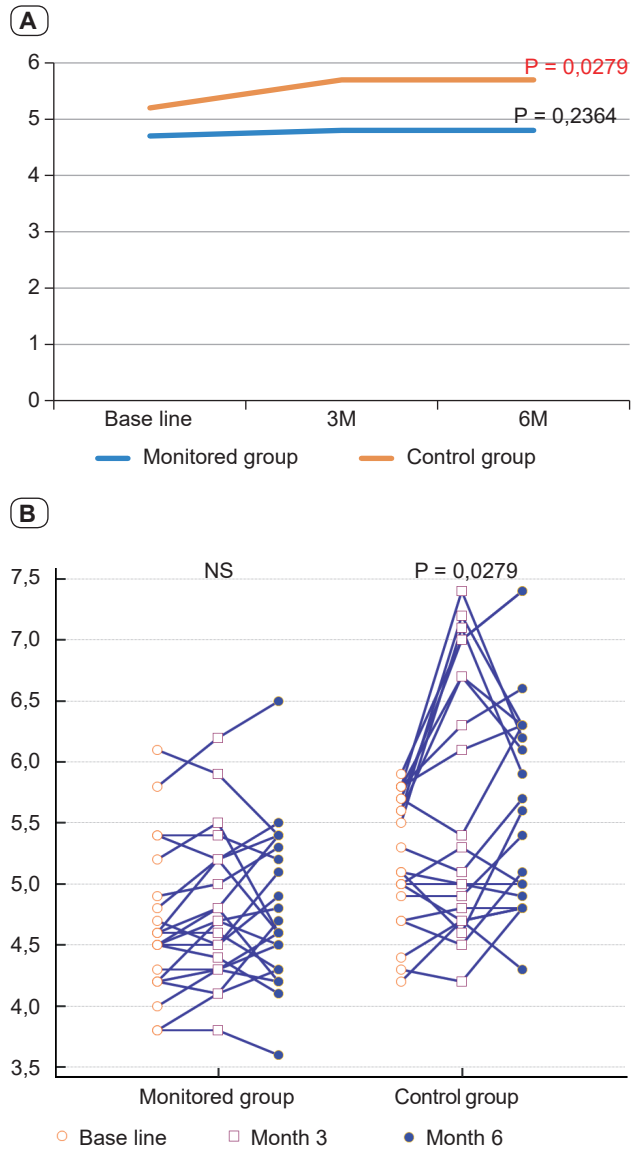

Fig. 2. Development of fasting glucose during the study period – A: whole group B: individually. M – month; NS – nonsignificant.

Discussion

Insulin resistance is a strong risk factor for the development of PTDM and cardiovascular diseases, which significantly affects the long-term survival of patients after KT. Modifiable factors, such as weight gain in the absence of regular physical activity, contribute significantly to insulin-resistant patients, much more frequently than their peers in the general population (6).

Several studies have verified that regular physical activity is an effective tool for the prevention and treatment of pre-diabetic diseases and type 2 DM, clearly strengthening its position among interventional procedures in this group of patients (17, 18). In contrast, in the transplanted population, data were severely limited. In 2008, Sharif et al. were the first to monitor the effects of intensive lifestyle modifications in KT patients. Physical activity included two hours of endurance discipline per week. However, the study was designed primarily for therapeutic purposes as the subjects had already been diagnosed with IGT or PTDM. At 6 months of follow-up, there was a 15% improvement in 2 hours postprandial glycemia versus a 12% deterioration in the control group. In the first group, 44% of those treated with IGT developed normal glucose tolerance, whereas only 4% switched to PTDM, and 58% of those monitored with PTDM achieved improvement (29% to IGT, 29% to normal tolerance). This study highlights the importance and significance of active intervention in the lifestyle of these patients, both in the prevention of high-risk patients and in the treatment of already developed PTDM. However, the evaluation of sporting activity is subjective (19).

Recently, a prospective randomized study compared the glycemic benefits of active versus passive lifestyle interventions in kidney allograft recipients (CAVIAR), comparing the effects of a complex lifestyle change on glucose metabolism among patients after KT without PTDM. A total of 130 recipients were randomized 1:1 into the active (lifestyle counseling by a renal dietitian using a behavior change technique) and passive intervention groups. As in our study, the follow-up duration was 6 months. In terms of physical activity, the patients were encouraged to increase their performance and maintain a training diary. This study did not confirm the different effects of active and passive interventions on insulin sensitivity or secretion (20). The Dutch multicenter randomized study Active Care after Transplantation (ACT) is currently underway, comparing three groups of patients (classic care, physical exercise intervention, and a combination of diet and exercise) with the main objective of assessing the impact of lifestyle changes on quality of life, as well as the degree of physical condition, adipose tissue, and cardiometabolic risk factors such as blood pressure, lipids, and glucose metabolism (21).

Weight gain and obesity are known risk factors for IR development during the post-transplant period. Oterdoom et al stated that obesity evaluated by the BMI index, as well as the distribution of adipose tissue determined by the waist-hip ratio, are the strongest determinants for the development of IR after KT. The distribution of adipose tissue is a risk factor independent of general obesity; therefore, the assessment of waist circumference provides more accurate information on abdominal obesity than BMI (6). In our study, regular physical activity led to a significant reduction in waist circumference and LDL cholesterol levels compared to the control group. In the CAVIAR study, the active intervention group achieved significant progress in reducing weight and fat mass compared with the passive group, which clearly contributed to improving the cardiometabolic risk profile of these patients (20). We also demonstrated a significant difference in the reduction of the waist circumference value between patients in the intervention group, which was achieved by the subgroup with the highest level of physical activity, supporting a direct relationship between the degree of physical activity and cardiometabolic risk. In 2011, Zelle et al conducted a prospective study in 540 recipients after KT and confirmed a strong independent correlation between low physical activity and cardiovascular and overall mortality (22). Recently, Byambasukh et al. published a study in which recipients who performed moderate-to high-intensity physical activity showed significantly lower cardiovascular and overall mortality than recipients with a sedentary lifestyle regardless of age, sex, and graft function (23).

The secondary objective of this study was to evaluate the influence of physical activity on graft function. We found a significantly lower serum creatinine level and a higher eGFR in the third month after the beginning of follow-up in the intervention group than in the control group. We assumed that the follow-up duration was relatively short in terms of the impact assessment of graft function. Italian authors Totti et al. reported a significant increase in creatinine and a decrease in eGFR during the 3-year follow-up period in the passive group compared to patients who exercised regularly ≥ at 150 min/week (24).

In our study, we confirmed that moderate-intensity regular exercise of at least 150 min/week is sufficient to adequately prevent glucose metabolism disorders associated with insulin resistance. This conclusion is in line with the ADA recommendations for high-risk patients or prediabetes to prevent and delay the development of DM (15). The World Health Organization (WHO) proposed the same minimum weekly limit for sports activity in its 2010 recommendations for the adult population. At the same time, they state that to achieve an additional health effect, it is necessary to increase this activity to ≥ 300 minutes of medium intensity per week or ≥ 150 minutes of high intensity per week (25). In our study, such an effect (significant reduction in waist circumference) was achieved by a subgroup that met the criteria of high-intensity and long-lasting exertion (≥ 300 min/week). In most available studies, an aerobic type of sport was used to

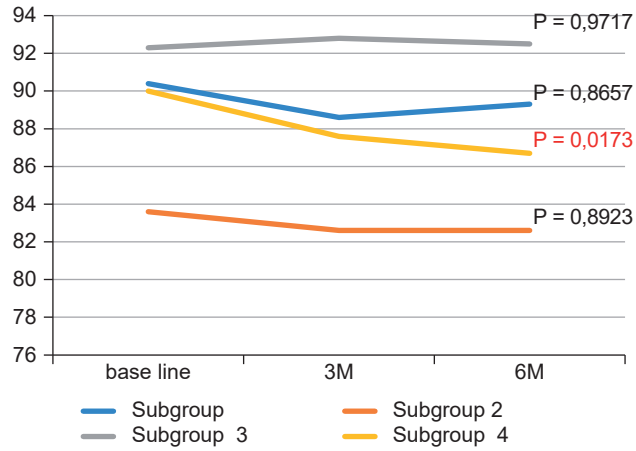

Fig. 3. Development of waist circumference in each subgroup during study period (according to activity level). TAG – triglycerides; M – month.

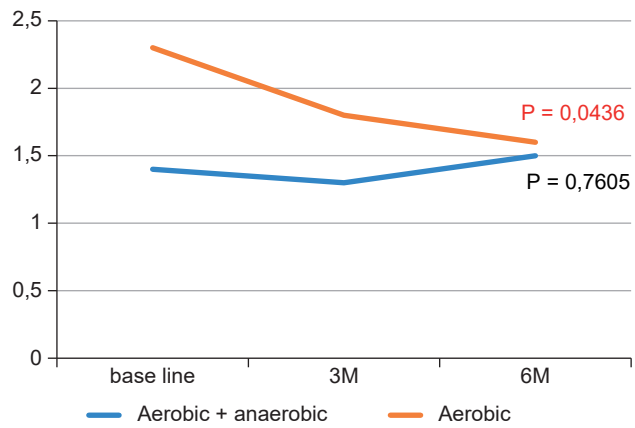

Fig. 4. Development of triglycerides in each subgroup during study period (according to the type of activity)

evaluate the effect of physical activity. Both aerobic and strength training are known to promote skeletal muscle, adipose tissue, and liver adaptation, in association with increased insulin action (13). The combination of endurance and strength training can provide even greater improvement and appears to be superior to continuous aerobic training (26). The ADA and WHO recommend incorporating a strength component into regular training (15, 25). By comparing the combined activity with aerobic conditions, we found no additional impact on the glucose metabolism parameters or anthropometric data. At the end of the follow-up period, the group with isolated aerobic activity showed significantly lower triglyceride levels.

There are several similarities between glucose metabolism disorders in the general population and those that arise de novo after KT. However, the transplanted population is exceptional in many aspects and needs to be approached individually. Therefore, there are no specific suggestions for the prevention or non-pharmacological treatment of these disorders in the general recommendations for recipient care after KT, especially at a time when KT patients are not rare in the population and a healthy lifestyle is the number one topic in most age groups. Based on these findings, we consider it necessary to apply regular physical activity and dietary counseling in daily practice as much as possible to improve the long-term survival of grafts and patients after KT.

We consider the incorporation of digital technologies for patient monitoring, and thus, the simple verification of data, which in our case is not based only on the questionnaire method, which is an important and unique aspect of this study. Sports bracelets, which in most cases are already part of the watch, are now widely available and are commonly used by beginners and professional athletes of various ages. They used motion- and thermally controlled sensors to record energy expenditure and monitor metabolic physical activity, providing an objective evaluation of each patient's athletic performance. When pairing them with a mobile application, we obtained a detailed analysis of the entire period under review, and, on the other hand, we consider them to be an important factor in motivating individuals and striving to improve their results. To date, no study has been performed on transplanted patient samples to objectively evaluate the impact of physical activity on changes in glucose metabolism. We consider this an excellent opportunity to further monitor the impact of lifestyle modifications on the development of cardiometabolic profiles in this risk group of patients. The possible different impact of lifestyle adjustments depending on sex remains questionable, given that a study in 2019 by Dedinská et al found that in men after KT, IR and metabolic syndrome were the main predictors of PTDM, while pancreatic b cell dysfunction (27). Therefore, it is necessary to incorporate this important variable in future research.

The limitations of the study are the small number of enrolled patients and the possible problem of monitoring physical activity in the control group. There was a significant difference in the time from kidney transplantation between the groups with worse kidney function; however, there were no differences in immunosuppression, and the average kidney function was excellent in both the groups. This limitation might also be due to the missing correction to prevent false discovery rates.

Conclusions

Performing Regular physical activity leads to a significant reduction in IR development after KT. To achieve this goal, it was necessary to complete at least 150 min of medium-intensity physical effort per week. Isolated aerobic and combined sports (aerobic + strength) appear to be equally effective.

After KT, patients are at an increased risk of developing IGT and PTDM, which is reflected in their high incidence in the given population. Therefore, in each transplant patient, it is necessary to examine the parameters of glucose metabolism, including the oral glucose tolerance test (oGTT), with the initiation of aggressive lifestyle modifications in patients with prediabetic disease or PTDM. However, it is extremely important that patients with normal glucose tolerance receive sufficient attention and that emphasis on lifestyle (especially regular physical activity) is a cornerstone of prevention, as in the general population.

References

1. Hjelmesaeth J, Midtvedt K, Jenssen T et al. Insulin resistance after renal transplantation: impact of immunosuppressive and antihypertensive therapy. Diabetes Care 2001; 24: 2121–2126.

2. Dedinská I, Baltesová T, Beňa L et al. Incidence of Diabetes Mellitus After Kidney Transplantation in Slovakia: Multicentric, Prospective Analysis. Transplantation Proceedings 2016; 48: 3292–3298.

3. Jorgensen MB, Hornum M, van Hall G et al. The impact of kidney transplantation on insulin sensitivity. Transpl Int 2017; 30295–30304.

4. Sharif A, Cohney S. Post-transplantation diabetes – state of the art. Lancet Diabetes Endocrinol 2016; 4: 337–349.

5. Ormazabal V, Nair S, Elfeky O et al. Association between insulin resistance and the development of cardiovascular disease. Cardiovasc Diabetol 2018; 17: 122.

6. Oterdoom LH, de Vries AP, Gansevoort RT et al. Determinants of insulin resistance in renal transplant recipients. Transplantation 2007; 83: 29.

7. Valderhaug TG, Hjelmesaeth J, Hartmann A et al. The association of early post- transplant glucose levels with long-term mortality. Diabetologia 2011; 54: 1341–1349.

8. Knowler WC, Fowler SE, Hamman RF et al. 10-Year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. Lancet 2009; 374: 1677–1686.

9. Li G, Zhang P, Wang J et al. The long-term effect of lifestyle interventions to prevent diabetes in the China Da Qing Diabetes Prevention Study: a 20-year follow-up study. Lancet 2008; 371: 1783–1789.

10. Masajtis-Zagajewska A, Muras K, Nowicki M et al. Effects of a Structured Physical Activity Program on Habitual Physical Activity and Body Composition in Patients With Chronic Kidney Disease and in Kidney Transplant Recipients. Exp Clin Transplant. 2019; 17 (2): 155–164.

11. O'Hare AM, Towney K, Bacchetti P et al. Decreased survival among sedentary patients undergoing dialysis: results from the dialysis morbidity and mortality study wave 2. Am J Kidney Dis 2003; 41 (2): 447–454.

12. Carvalho EV, Reboredo MM, Gomes EP. Physical activity in daily life assessed by an accelerometer in kidney transplant recipients and hemodialysis patients. Transplant Proc 2014; 46 (6): 1713–1717.

13. Roberts CK, Hevener AL, Barnard RJ. Metabolic syndrome and insulin resistance: underlying causes and modification by exercise training. Compr Physiol 2013; 3: 1–58.

14. Kasiske BL, Zeier MG, Chapman JR et al. KDIGO clinical practice guideline for the care of kidney transplant recipients: A summary. Kidney Int 2009; 9 (Suppl 3): 1– 155.

15. Colberg SR, Sigal RJ, Yardley JE et al. Physical Activity/Exercise and Diabetes: A Position Statement of the American Diabetes Association. Diabetes Care 2016; 39 (11): 2065–2079.

16. American College of Sports Medicine. ACSM's Guidelines for Exercise Testing and Prescription. 7th ed. Baltimore, MD: Lippincott Williams & Wilkins; 2006.

17. Sanz C, Gautier JF, Hanaire H. Physical exercise for the prevention and treatment of type 2 diabetes. Diabetes Metab. 2010; 36 (5): 346–351.

18. Chakkera HA, Weil EJ, Awanson CM et al. Pretransplant risk score for new-onset diabetes after kidney transplantation. Diabetes Care 2011; 34(10): 2141–2145.

19. Sharif A, Moore R, Baboolal K. Influence of lifestyle modification in renal transplant recipients with postprandial hyperglycemia. Transplantation 2008; 85: 353–358.

20. Kuningas K, Driscoll J, Mair R et al. Comparing glycaemic benefits of active versus passive lifestyle intervention in kidney allograft recipients (CAVIAR): a randomised controlled trial. Transplantation 2020; 104 (7): 1491–1499.

21. Klaassen G, Zelle DM, Navis GJ et al. Lifestyle intervention to improve quality of life and prevent weight gain after renal transplantation: design of the active care after transplantation (ACT) randomized controlled trial. BMC Nephrol 2017; 18: 296.

22. Zelle DM, Cerpeleijn E, Stolk RP. Low physical activity and risk of cardiovascular and all-cause mortality in renal transplant recipients. Clin J Am Soc Nephrol 2011; 6 (4): 898–905.

23. Byambasukh O, Osté MC, Gomes-Neto AW et al. Journal of Clinical Medicine 2020; 9 (2): 415.

24. Totti V, Fernhall B, Di Michele R et al. Medicina 2020; 56 (4): 183.

25. WHO. Global recommendations on physical activity for health 2010. https: //www.who.int/dietphysicalactivity/publications/9789241599979/en/.

26. Jelleyman C, Yates T, O'Donovan G et al. The effects of high-intensity interval training on glucose regulation and insulin resistance: a meta-analysis. Obes Rev 2015; 16: 942–961.

27. Dedinská I, Graňák K, Vnučák M et al. Role of sex in post-transplant diabetes mellitus development: are men and women equal? J Diabet Complications 2019; 33 (4): 315–322.

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